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Application No.: 10/814,981  
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Atty Docket No.: INTEL1490(P18518)

**Amendments to the Claims**

Please amend claims 1, 22, 26 and 31 as indicated below.

The listing of claims will replace all prior versions, and listings of claims in the application:

**Listing of Claims:**

1. (Currently Amended) A method to detect binding of a first specific binding pair member to a second specific binding pair member, comprising:
  - a) associating a first specific binding pair member with a surface-enhanced Raman scattering-active particle or substrate;
  - b) contacting the first specific binding pair member associated with the surface-enhanced Raman scattering-active particle or substrate with a second specific binding pair member; and
  - c) detecting binding of the second specific binding pair member to the first specific binding pair member by detecting a difference in a surface-enhanced Raman scattering signal of the first specific binding pair member before contacting the first specific binding pair member with the second specific binding pair member and after contacting the first specific binding pair member with the second specific binding pair member, wherein the surface-enhanced Raman scattering signal is generated by excitation of the first specific binding pair member associated with the surface-enhanced Raman scattering-active particle or substrate, thereby detecting binding of the first specific binding pair member to the second specific binding pair member.
2. (Original) The method of claim 1, wherein the surface-enhanced Raman scattering-active particle or substrate associated with the first specific binding pair member is a metal particle.
3. (Original) The method of claim 2, wherein the first specific binding pair member is associated with the metal particle by adsorbing the first specific binding pair member to the surface-enhanced Raman scattering surface.

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4. (Original) The method of claim 3, wherein the metal particle comprises colloidal silver or gold.
5. (Original) The method of claim 3, wherein the first specific binding pair member is immobilized on an immobilization substrate prior to associating with the surface-enhanced Raman scattering-active surface.
6. (Original) The method of claim 1, wherein the difference in the surface-enhanced Raman scattering signal is a decrease in the signal.
7. (Original) The method of claim 6, wherein binding of the second specific binding pair member to the first specific binding pair member dissociates the first specific binding pair member from the metal particle.
8. (Original) The method of claim 1, wherein the difference in the surface-enhanced Raman scattering signal is an increase in the signal.
9. (Original) The method of claim 3, wherein adsorption is detected before the second specific binding pair member is contacted with the first specific binding pair member.
10. (Original) The method of claim 9, wherein adsorption is detected by detecting an increase in a surface-enhanced Raman scattering signal generated by the first specific binding pair member after contacting the first specific binding pair member with the metal particle.
11. (Original) The method of claim 3, wherein the first specific binding pair member is associated with the metal particle in the presence of a chemical salt.
12. (Original) The method of claim 11, wherein the chemical salt is lithium chloride.
13. (Original) The method of claim 1, wherein the first specific binding member is a protein and the second specific binding pair member is a protein.

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14. (Original) The method of claim 13, wherein the first or second specific binding pair member is an antibody molecule, or fragment thereof.
15. (Original) The method of claim 1, wherein the first specific binding pair member is a receptor and the second specific binding pair member is a ligand.
16. (Original) The method of claim 1, wherein the first or second specific binding pair member is a nucleic acid molecule and the other of the first or second specific binding pair member is a protein.
17. (Original) The method of claim 13, wherein the first specific binding pair member is bound to a surface-enhanced Raman scattering label.
18. (Original) The method of claim 17, wherein the surface-enhanced Raman scattering label is deoxy-adenosine monophosphate.
19. (Original) The method of claim 18, wherein surface enhanced coherent anti-Stokes Raman spectroscopy is used to detect the first specific binding pair member.
20. (Original) The method of claim 1, wherein the first specific binding pair member is associated with the surface-enhanced Raman scattering-active particle or substrate by immobilizing the first specific binding pair member on a surface-enhanced Raman scattering-active substrate.
21. (Original) The method of claim 20, wherein the surface-enhanced Raman scattering-active substrate comprises a porous silicon substrate comprising impregnated metals.
22. (Currently Amended) A method to detect binding of an antibody, or fragment thereof, to an antigen, comprising:

a) immobilizing an antibody on an immobilization substrate;  
b) contacting the immobilized antibody with a metal particle to adsorb the immobilized antibody on the metal particle;  
c) contacting the immobilized antibody with an antigen; and  
d) detecting binding of the antigen to the antibody, or fragment thereof, by detecting a difference in a surface-enhanced Raman scattering signal generated by the antibody before contacting the antibody with the antigen and after contacting the antibody with the antigen, wherein the surface-enhanced Raman scattering signal is generated by excitation of the surface-enhanced Raman scattering-active particle or substrate, thereby detecting binding of the antibody to the antigen.

23. (Original) The method of claim 22, wherein the antibody, or fragment thereof, is a whole antibody molecule.

24. (Original) The method of claim 22, wherein the antibody, or fragment thereof, is a Fab fragment.

25. (Original) The method of claim 22, wherein the metal particle comprises colloidal gold or silver.

26. (Currently Amended) A method to detect an analyte in a biological sample, comprising:

- a) immobilizing a first specific binding pair member on a surface, wherein the first specific binding pair member binds the analyte;  
b) contacting the immobilized first specific binding pair member with a metal particle to adsorb the immobilized first specific binding pair member on the metal particle;  
c) contacting the immobilized first specific binding pair member adsorbed on the metal particle with the biological sample; and  
d) detecting a surface-enhanced Raman scattering signal generated by excitation of the metal particle adsorbed by the immobilized first specific binding pair member before contacting

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the immobilized first specific binding pair member with the second specific binding pair member and after contacting the first specific binding pair member with the second specific binding pair member, wherein a difference in the detected surface-enhanced Raman scattering signals is indicative of the presence of the analyte in the biological sample.

27. (Original) The method of claim 26, wherein the first specific binding pair member is an antibody, or fragment thereof.

28. (Original) The method of claim 26, wherein the metal particle comprises colloidal gold or silver.

29. (Original) The method of claim 26, wherein the first specific binding pair member is adsorbed on the metal particle in the presence of lithium chloride.

30. (Original) The method of claim 26, wherein the biologic sample comprises serum.

31. (Currently Amended) A method to detect an antibody or a fragment thereof, comprising:

- a) immobilizing the antibody, or fragment thereof, on a surface;
- b) contacting the antibody, or fragment thereof, with a metal particle to adsorb the immobilized antibody on the metal particle; and
- c) detecting a surface-enhanced Raman scattering signal generated by excitation of the metal particle adsorbed by ~~of~~ the immobilized antibody, or fragment thereof, thereby detecting the antibody, or fragment thereof.

32. (Original) The method of claim 30, wherein the antibody, or fragment thereof, is a whole antibody molecule.

33. (Original) The method of claim 30, wherein the antibody, or fragment thereof, is a Fab fragment.

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34. (Original) The method of claim 30, wherein the metal particle comprises colloidal gold or silver.